8. (Twice Amended) The method according to claim 1 or 2, wherein the antibody directed against AAV-2 is DSM ACC2194.

THE REMARKS

The Amendments

Claim 5 is amended to delete the trademark name and replace it with a generic name.

Claim 8 is amended to delete "A20."

No new matter is added in any of the above amendment and the Examiner is respectfully requested to enter the amendments and reconsider the application.

The Response

Claims 1-9 are pending.

1. Objection to the Specification

The specification was object to on informalities. Applicants are submitting herewith a substitute application pursuant to 37 C.F.R. §1.125(a). Also enclosed are a marked-up version of the specification and a marked-up version of the claims showing all the changes made.

2. Objection to drawings

The drawings were objected to for informalities. Applicants are hereby submitting a new set of drawings addressing the issues.

3. 35 U.S.C. §112, Second Paragraph Rejection

Claims 1, 2 and 8 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner states that the claims are rendered indefinite in that they only describe the composition by an arbitrary name "A20." Applicants respectfully submit that Claims 1 and 2 do not recite "A20," therefore, Claims 1 and 2 are not indefinite. Applicants have amended Claim 8 to delete "A20" to overcome the rejection.

Claims 1, 2 and 5 are rejected for allegedly containing a trademark/trade name. Applicants respectfully submit that Claims 1 and 2 do not contain a trademark or tradename. Claim 5 is amended to change "Sepharose®" to agarose.

Therefore, the §112 rejection of Claims 1, 2, 5 and 8 should be withdrawn.

4. 35 U.S.C. §112, First Paragraph Rejection

Claims 1, 2 and 8 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner states that there is no indication in the specification as to public availability of DSM ACC 2194. The undersigned attorney of record hereby states that the instant invention will be irrevocable and without restriction released to the public upon the issuance of a patent. Therefore, the §112, first paragraph rejection of Claims 1, 2 and 8 should be withdrawn.

5. 35 U.S.C. §103(a) rejections

Claims 1-9 are rejected under 35 U.S.C. §103(a) as being unpatentable over Shimada, *et al.* (WO 96/29349) and Wistuba, *et al.* (Journal of Virology, Sept. 1995) and further in view of Harlow (Antibodies, a laboratory manual, 1988).

According to the present purification method, AAV-2 or antigen portions thereof are eluted from the chromatographic material/antibody by a solution containing 0.5 to 4.5 M $MgCl_2$.

The advantage of the present method is that the immobilized antibody is not denatured or separated from the column during the elution of AAV-2, but continues to be bonded to the column, so that the column can be used several times after its regeneration. Furthermore, the purified viruses remain stable and infectious. (See Page 3, 3rd paragraph)

Shimada, *et al.*, disclose a monoclonal antibody specifically recognizing adeno-associated virus CAP protein. The specific monoclonal antibody can be used for the detection of an adeno-associated virus and the purification of adeno-associated virus vectors for gene therapy. The reference does not teach or suggest an elution condition of 0.5 to 4.5M $MgCl_2$, which is the

feature of the present invention. Further, the reference does not teach an antibody specific to AAV-2.

Wistuba, *et al.*, disclose the immunoprecipitation of Rep proteins by antibody A20. The reference does not teach or suggest an elution condition as recited in Claim 1.

Harlow, *et al.*, disclose strategies for testing elution conditions for an immunoaffility purification. At page 551, the reference states that "there are no good shortcuts nor any guaranteed useful buffers. The best strategy is to test small antibodies in elution conditions as possible."

The reference also discloses: "If trying for the gentlest elution conditions, start with acid conditions first, then check basic elution buffers. If these conditions do not elute the antigen, try others. A general order to check the various conditions would be: acid, pH 3-1.5; base pH 10-12.5; $MgCl_2$, 3-5 M; LiCl 5-10 M; water; ethylene glycol 25-50%; dioxane 5-20%, thiocyanate 1-5 M; guanidine 2-5 M; urea 2-8 M; SDS 0.5% to 2%." (Page 551)

There is no suggestion in Harlow, *et al.*, as to purifying and concentrating AAV-2 by immunoaffility purification using an elution condition of 0.5 to 4.5M $MgCl_2$. Applicants respectfully submit that the Examiner is not allowed to use hindsight construction using Applicants' invention as a blueprint to pick and choose different elements from different references to produce the claimed invention.

Therefore, the §103(a) rejection of Claims 1-9 should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, the Applicants believe the application is in good and proper condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is

encouraged to call the undersigned at (650) 463-8109. A telephone conference is especially requested if the Examiner intends to maintain the present rejections.

Respectfully submitted,

Date: March 10, 2003

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MARKED-UP VERSION TO SHOW CHANGES MADE TO CLAIMS

1. (Twice Amended) A method for purifying and concentrating AAV-2 and antigen portions thereof from a sample, said method comprising the steps of:

binding AAV-2 or antigen portions thereof to an activated chromatographic material which comprises antibodies linked thereto and directed against AAV-2, and

eluting said AAV-2 or antigen portions thereof using a solution containing 0.5 to 4.5 [m]M $MgCl_2$.

2. (Reiterated) The method according to claim 1, wherein said AAV-2 is a wildtype AAV-2 or a recombinantly prepared AAV-2.

3. (Reiterated) The method according to claim 1 or 2, wherein the chromatographic material is selected from the group consisting of agarose gels, dextran gels, cellulose gel matrices and acrylamide gel matrices.

4. (Reiterated) The method according to claim 1 or 2, wherein the chromatographic material carries a ligand suitable for binding proteins.

5 (Twice Amended) The method according to [claim 1 or 2] 3, wherein the chromatographic material is CNBr-activated [sempharose®] agarose or NHS-activated [sempharose®] agarose.

6. (Reiterated) The method according to claim 1 or 2, wherein the solution contains 2 to 3 M $MgCl_2$.

7. (Reiterated) The method according to claim 1 or 2, wherein the sample containing the AAV-2 is a cell culture supernatant or cell extracts.

8. (Twice Amended) The method according to claim 1 or 2, wherein the antibody directed against AAV-2 is [A20 (DSM ACC2194)] DSM ACC2194.

9. (Reiterated) A kit for carrying out the method according to claims 1 or 2, comprising

an antibody directed against AAV-2, and

conventional auxiliary agents selected from the group consisting of buffers, chromatographic material and controls.

CLEAN VERSION OF AMENDED PARAGRAPHS

In the Specification

Page 1, line 3, before "The present invention":

This application is a continuation of U.S. Application No. 09/508,037, filed June 23, 2000, which was the National Stage of International Application PCT/DE98/02569, filed September 1, 1998; which claims the priority of DE 197 38 292.4, filed September 2, 1997.